REMARKS

Claims 1 and 3-18 are pending and claims 19-40 are withdrawn as directed to a non-elected species. Claim 2 was previously cancelled.

35 U.S.C. § 112, Second Paragraph

Claims 1 and 3-18 are rejected under 35 U.S.C. §112, second paragraphs, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter the Applicant regards as the invention. Specifically, the Examiner alleges that the phrase "stem cells derived from neural tissue" is not clear in indicating how the Applicant intends for the neural cells to be derived from neural tissue.

The Applicant intends the standard English meaning of "derive" to be applied, *i.e.*, to obtain or receive from a source. *Dictionary.com. The American Heritage Dictionary of the English Language, Fourth Edition. Houghton Mifflin Company*, 2004. http://dictionary.reference.com/browse/derived (accessed: January 9, 2008)). The American Heritage Dictionary also provides a definition for the word "derive" in a chemistry context, *i.e.*, to produce or obtain (a compound) from another substance by chemical reaction. *Id.* The Office Action indicates, however, that the word "derived" has been interpreted as "derivative" and that the starting material is "derivatized." The Office Action further suggests that the rejection could be overcome by substituting the words "isolated" or "obtained" for the word "derived." The Applicant does not believe such a substitution is necessary because, as indicated above, the word "derive" is defined as "to obtain or receive from a source" and the concept of a derivative is not suggested. Thus, the Applicant's choice of language and the Examiner's understanding actually correspond, and no change is required. For this reason, the Applicant requests that the rejection be withdrawn.

35 U.S.C. § 112, First Paragraph

Claims 1, 3-4 and 10-18 are rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to enable "a method of producing oligodendrocytes from all types of neural stem cells isolated from any mammal at any developmental stage while the cells are located in a mammal other than a rodent (i.e., humans)." Specifically, the Examiner alleges that the Declaration Under 37 C.F.R. § 1.132 by Samuel Weiss ("First Weiss Declaration") submitted previously "does not provide sufficient evidence for producing oligodendrocytes comprising contacting multipotent neural stem cells in any other mammal other than a rodent (i.e. human) using any other oligodendrocyte promoting factor." Office Action mailed October 15, 2007 at p. 5.

To satisfy the enablement requirement of 35 U.S.C. §112, first paragraph, there must be sufficient disclosure to teach one of ordinary skill in the art to make and use the invention as broadly as it is claimed. The present specification teaches methods of producing oligodendrocytes from mammalian multipotent neural stem cells and demonstrates that the olgodendrocytes are produced *in vitro*. Further, the Applicant has provided further evidence, in the form of the First Weiss Declaration, that the claimed methods also produce oligodendrocytes from mammalian multipotent neural stem cells in mice, a standard animal model. Accordingly, the specification fully teaches one of skill in the art how to make and use the invention.

The Applicant provided evidence in the First Weiss Declaration that the claimed compounds are effective at producing oligodendrocytes in an animal model. Specifically, the data presented in the First Weiss Declaration demonstrated that administration of GM-CSF increases the production of new oligodendrocytes in CD1 male mice many fold. Further, the Applicant has provided in Examples 1-4 of the specification data showing the same effect *in vitro*. The Applicant provides herewith a second Declaration Under 37 C.F.R. § 1.132 by Samuel Weiss ("Second Weiss Declaration") stating that mouse animal models are accepted models for the evaluation of multipotent neural stem cells.

The Federal Circuit has held that evidence showing that compounds within the scope of the claims that exhibit a recited activity *in vivo* "should [be] sufficient to satisfy the applicants' burden." *In re Brana,* 51 F. 3d 1560, 1567 (Fed. Cir. 1995). While *In re Brana* specifically

related to antitumor therapies and animal tumor models, one can reasonably extrapolate the findings to pertain to any novel therapeutic that is being tested in standard animal models of human disease. Therefore, the demonstration by the Applicant that the recited oligodendrocyte promoting factors promote the production of oligodendrocytes from multipotent neural stem cells both *in vitro* and *in vivo* in an accepted animal model is sufficient to establish the enablement of the present claims.

In the cited cases, the Federal Circuit further addressed a contention that "*in vivo* tests in animals ... are not reasonably predictive of success in humans" by finding that this assertion confused "the requirements under law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption." *Id.* The Court found that "proof of an alleged pharmaceutical property of a compound by statistically significant tests with standard experimental animals is sufficient to establish utility." *Id.* (citing *In re Krimmel*, 292 F.2d 948 (CCPA 1961)). The Court indicated that "[w]e hold as we do because it is our firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment in humans." *Id.* at 1567 (*citing In re Krimmel*, 292 F.2d 948 (CCPA 1961) (emphasis added).

The Applicant has shown that the claimed molecules are pharmacologically active in an accepted animal model. Therefore, Applicant's disclosure satisfies the enablement standard.

The Office indicates that the State of the Art as alleged to be indicated by Chandran and Compston indicates that interspecies differences in oligodendrocyte potential of neural precursors cautions the extent to which data from rodents can be reliably made to humans. However, as discussed, the Office Action has set forth a much more rigorous standard, *i.e.*, demonstrated efficacy in humans, than is required by the Federal Circuit. The present application meets the standard set by the Federal Circuit of a demonstrated efficacy in a standard animal model. More cannot be required by the Patent Office.

The Office Action further indicates that the art indicates unpredictability as alleged to be indicated by Imitola et al. ("Imitola"). Imitola, a review article, is stated in the Office Action to "caution that careful strategic planning and extensive animal testing will be required before

clinical studies can be entertained" and that "more research is needed to understand the signaling pathways for obtaining highly specific molecular targets without inducing aberrant neurogenesis or tumorigenic proliferation." Office Action mailed October 15, 2007 at p. 7. However, as pointed out above, the Federal Circuit is willing to accept that a compound that exhibits a desirable pharmaceutical property in a standard experimental animal may not eventually have value in the treatment of humans. Thus, a lack of human data does not preclude patentability and such data cannot be required by the Patent Office.

The Office Action also indicates that because of the alleged unpredictability demonstrated by the art, undue experimentation would be required to practice the invention. Such arguments have previously been addressed and dismissed by the Federal Circuit with regard to therapeutic compounds. Proof of human efficacy or FDA phase II testing is not required to meet § 112. *See In re Brana,* 51 F. 3d at 1568 (*citing Scott v. Finney*, 34 F. 3d 1058, 1063 (Fed. Cir. 1994)). "The stage at which an invention in this [pharmaceutical] field becomes useful is well before it is ready to be administered to humans." *Id.* at 1567. Requiring that a drug show efficacy in humans undermines the incentive to pursue patents in drugs in the first place because few companies if any could pursue the drug into phase II testing just to prove utility in humans. *Id.* "Usefulness in patent law, and in particular in the context of pharmaceutical inventions necessarily includes the expectation of further research and development." *Id.* The Applicant expects that human testing will be required to establish safety and efficacy prior to marketing the claimed compounds to produce oligodendrocytes from neural stem cells in humans; however, this form of research and development, *i.e.*, experimentation, is not considered undue or excessive by either the Federal Circuit or those skilled in the art. As set forth in the MPEP, "[t]here is no decisional law that requires an applicant to provide data from human clinical trials to establish utility for an invention related to treatment of human disorders, even with respect to situations where no art-recognized animal models existed for the human disease encompassed by the claims." MPEP § 2107.03(c) III (Rev. 5, Aug. 2006) (citations omitted).

Because the present specification enables the claimed methods, the Applicant requests that the rejection of claims 1, 3-4, and 10-18 under 35 U.S.C. § 112 be withdrawn.

Conclusions

For the reasons set forth above, the Applicant submits that the claims of this application are allowable. Reconsideration and withdrawal of the Examiner's rejections are hereby requested. Allowance of the claims remaining in this application is earnestly solicited. At a minimum, the Applicant requests entry of the Amendment so that the application is in condition for appeal.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at 404-892-5005.

No fees are believed to be due with this Amendment, however, please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 1-11-2008

Michael R. Asam
Reg. No. 51,417

Fish & Richardson P.C.
1180 Peachtree Street, N.E.
21st Floor
Atlanta, GA 30309
Telephone: (404) 892-5005
Facsimile: (404) 892-5002